MR Quantification of Flow in Children with Vein of Galen Malformations

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Summary

Vein of Galen vascular malformations are either Vein of Galen Aneurysmal malformations (VGAMs) or Vein of Galen Aneurysmal Dilatations (VGADs). VGAMs may be of the choroidal or mural type and are fistulas associated with the precursor of the vein of Galen.

The treatment of VGAMs is aimed at controlling the size of the vascular shunt since it is believed that the shunt is responsible for venous hypertension, cardiac stress, delayed development and may be so large as to damage the brain. In VGAMs as noted by Berenstein and Lasjaunias.

Absolute measures of flow may contribute to our understanding of CNS disease and permit objective measures of the success or failure of therapeutic interventions [5]. MR phase contrast cine angiographic techniques can be employed to measure bulk flow in intracranial vessels. Vein of Galen vascular malformations are an ideal model to measure venous flow as the draining vein is large and angiographic evaluation is limited. Thus our goal was to develop an objective non-invasive method of measuring vascular flow in VGAMs and VGADs [6]. Herein we report our experience using this technique in a group of patients with Vein of Galen vascular malformations. We also hypothesized that the degree of shunting would correlate to the degree of cardiac stress and be an indicator of optimal timing for intervention.

We believe that we have succeeded in our goal to develop an objective, non-invasive method of shunt quantification using velocity encoded MR sequences. This promises new insight into the hemodynamics, natural history and treatment response of vascular malformations.

Introduction

Vein of Galen vascular malformations are either Vein of Galen Aneurysmal malformations (VGAMs) or Vein of Galen Aneurysmal Dilatations (VGADs). VGAMs may be of the choroidal or mural type and are fistulas associated with the precursor of the vein of Galen, the medial vein of the prosencephalon [1] while VGADs are either dural shunts or parenchymal AVMs that drain into the vein of Galen. VGAMs present early in life with congestive heart failure (CHF), failure to thrive (FTT) and hydrocephalus, but are not prone to hemorrhage, while VGADs present later and have a significant risk of hemorrhage [2].

The treatment of VGAMs is aimed at controlling the size of the vascular shunt since it is believed that the shunt is responsible for venous hypertension, cardiac stress, delayed development and may be so large as to damage the brain. In VGAMs as noted by Berenstein and Lasjaunias, "The primary goal in neonates is obliteration of the major portion of the fistu-

Table 1 **Scan Parameters for VENC studies**

TR	varies with heart rate
TE	2.4-6.6 ms
FLIP ANGLE	30 degrees
FOV	30 or 40 cm
MATRIX	192 x200
PIXEL SIZE	1.6x1.5mm or 2.1x2mm
SLICE THICKNESS	4.7-6.8mm
AVERAGES	2
CARDIAC PHASES	20-45 per cardiac cycle (collected 2 RR intervals)
BANDWIDTH	15.63 KHz
GRADIENTS	27mT/meter & 72 mT/meter/ms shielded power gradients
VENC	50-600 mm/s (in slice)

Table 2 **Study types performed (n=5)**

CT	10
CTA	3
MR	20
MRA/MRV	19
MR Q FLOW	15
ANGIOGRAPHY	15
ULTRASOUND	4

la to allow resolution of the CHF. Since these patients cannot tolerate a significant volume load and usually have borderline renal function, the extent of angiographic evaluation must be limited[2]."

Non invasive imaging studies such as CTA and MRA have advanced rapidly over the previous few years. Less effort has been devoted to the quantification of cerebral blood flow in spite of the fact that such approaches have been a focus of cardiovascular MR imaging[3,4] and absolute measures of flow may contribute to our understanding of CNS disease and permit objective measures of the success or failure of therapeutic interventions[5]. MR phase contrast cine angiographic techniques can be employed to measure bulk flow in intracranial vessels. Vein of Galen vascular malformations are an ideal model to measure venous flow as the draining vein is large and angiographic evaluation is limited. Thus our goal was to de-

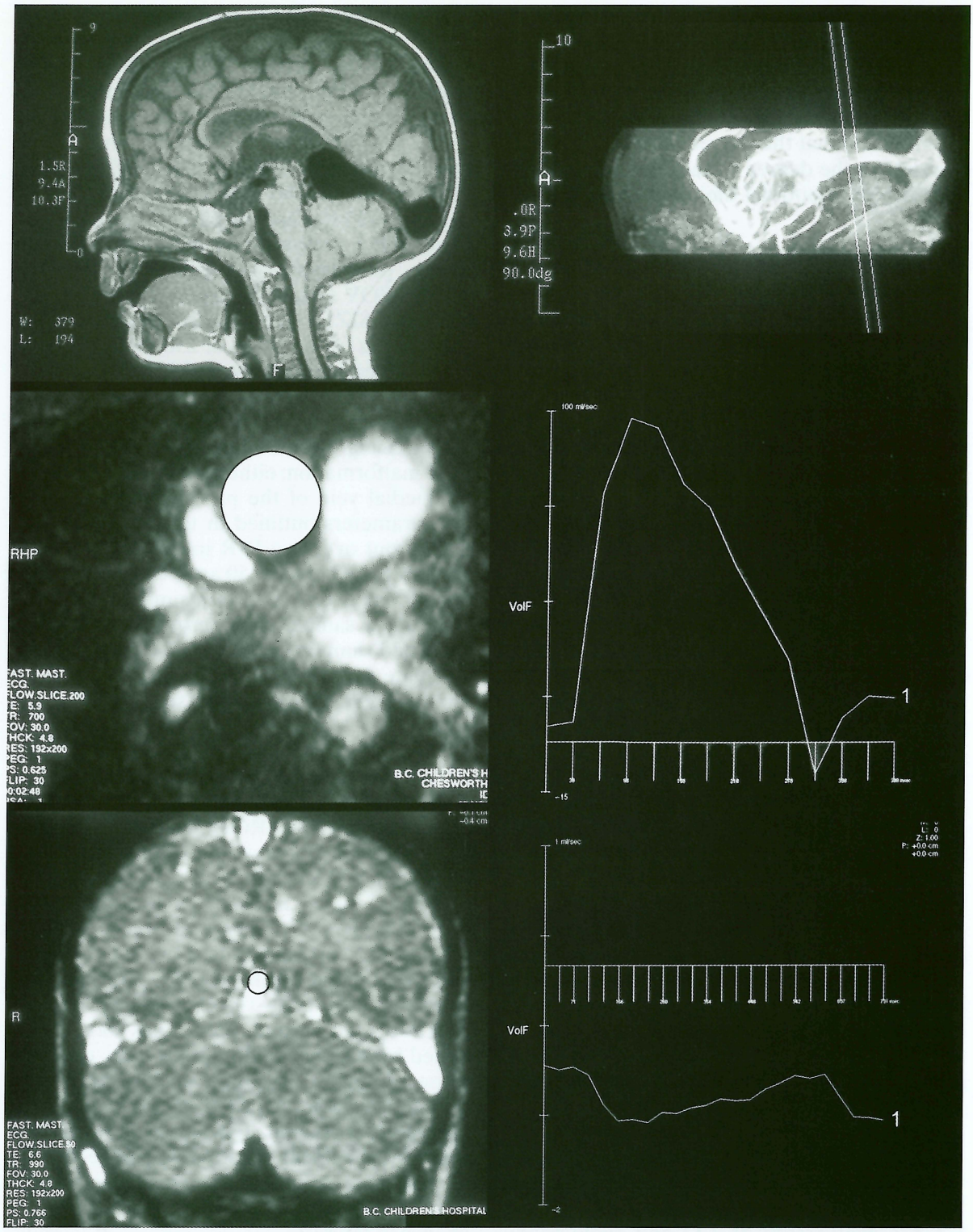


Figure 1 A) Upper left sagittal T1 MR sequence showing flow void of enlarged vein in a patient with a VGAM. Upper right-sided image is the corresponding MRA view used to place a volume for MR Q flow evaluation on the venous outlet. The middle image on the left is the magnitude image from the sample volume across the aorta (circled) used to evaluate cardiac output, which is plotted in the graph to the right of it. The lower image on the left is the magnitude image from the sample volume across the venous outlet of the malformation. The MR Q flow data from volume #1 is plotted in the graph to the right of it.

velop an objective non-invasive method of measuring vascular flow in VGAMs and VGADs [6]. Herein we report our experience using this technique in a group of patients with Vein of Galen vascular malformations. We also hypothesized that the degree of shunting would correlate to the degree of cardiac stress and be an indicator of optimal timing for intervention.

Material and Methods

All velocity encoded (VENC) MR studies (Q Flow) were carried out on a Picker 1.5 T HPQ or Edge system (Picker Int'l. Cleveland, Ohio) with a standard cardiac software package using prospective ECG gating. Before performing MR Q Flow studies on patients, we tested the accuracy of each sequence with flow phantoms [6]. The tested sequences were coherent gradient echo sequences (GRASS or FAST) with motion artifact suppression and ranged in velocity encoding from 50-600 cm/s Additional parameters are outlined in table 1.

A UHDC (University Hospital (London) Development Corporation, London, Canada) flow phantom that generates a range of continuous and pulsatile flows was employed to trial each sequence. The data was analyzed with the provided cardiac software package by two radiologists who were unaware of the selected flow rate, and the results compared to the known answer [1]. A similar approach was used for testing the sequences using an extra corporeal membrane oxygenation (ECMO) machine used for intra-operative cardiac bypass. In addition to the analysis described above, the volume of fluid pumped by the ECMO machine during the Q Flow testing was collected in a graduated cylinder and compared to the calculated value. From this preliminary work it was determined that an error of plus or minus 5% was expected in the flow range and size of vessels expected to be sampled in patients with Vein of Galen malformations.

Five patients, (four male, one female) with Vein of Galen vascular malformations have undergone serial studies with a combination of MR, MR angiography (MRA), MR Q Flow, CT, CT angiography (CTA) and angiography. Studies have been performed before, during and after treatment with an average range of clinical follow-up of six years and six months (table 2).

MR studies included routine sequences and 3D ToF MOTSA MRA. Imaging included axial, sagittal and/or coronal T1 weighted images 600/20/2/192x256, (TR/TE/AV/MATRIX SIZE), axial spin echo or fast spin echo T2 weighted images (2500-3500/40, 80/ 1-3/192x256) and a 3DT1 weighted sequence (24/4.4/2 mm/256x256). Incoherent gradient echo MRA sequences, (SPGR or RF-FAST) was usually placed in a transverse plane with a presaturation pulse using the following parameters: 42/6.9/20/20/ 0.9/180x180 (TR/TE/FOV / FLIP ANGLE / THICKNESS / MATRIX SIZE). The sequence included MTC (B1=800 Hz) at an offset of 2500 Hz, [7]. Imaging times ranged between ten and 12 minutes.

Either the MRA or the standard images were used to place velocity sensitive sequences perpendicular to the venous outflow of the vascular malformation; either the Vein of Galen or the medial vein of the prosencephalon. Using the parameters outlined in table 1, gating was carried out over two R-R intervals with multiple flow rates between 50 and 600 cm/s. Cardiac output was determined in a similar fashion by choosing a sample slice across the ascending aorta and sampling over two R-R intervals. An adequate data set was obtained when the slowest available flow sensitive sequence did not alias.

The flow data was analyzed with the provided cardiac software package by generating flow maps across the cardiac cycle. We defined the region of interest (ROI) by magnifying the magnitude image four-fold and setting the window width and levels at 50% of the maximal intraluminal signal intensity in the image. The ROI boundary was manually traced and applied to the corresponding flow map. The software calculated peak velocity, average flow rates per duty cycle (30-40 ms), and average flow rates per second. Flow rates were determined by adding the flow rates /duty cycle because of marked variation in flow during systole and diastole. All flow values were finally expressed in ml/min. The values derived from the slowest velocity sensitive sequence without aliasing were defined as the most reliable data.

The evaluation is outlined through a series of images in figure 1.

CT, CTA, and angiography were also performed as part of the patient's clinical evaluation. The CT and CTA studies were performed on a Siemens Somatom Plus scanner (Siemens,

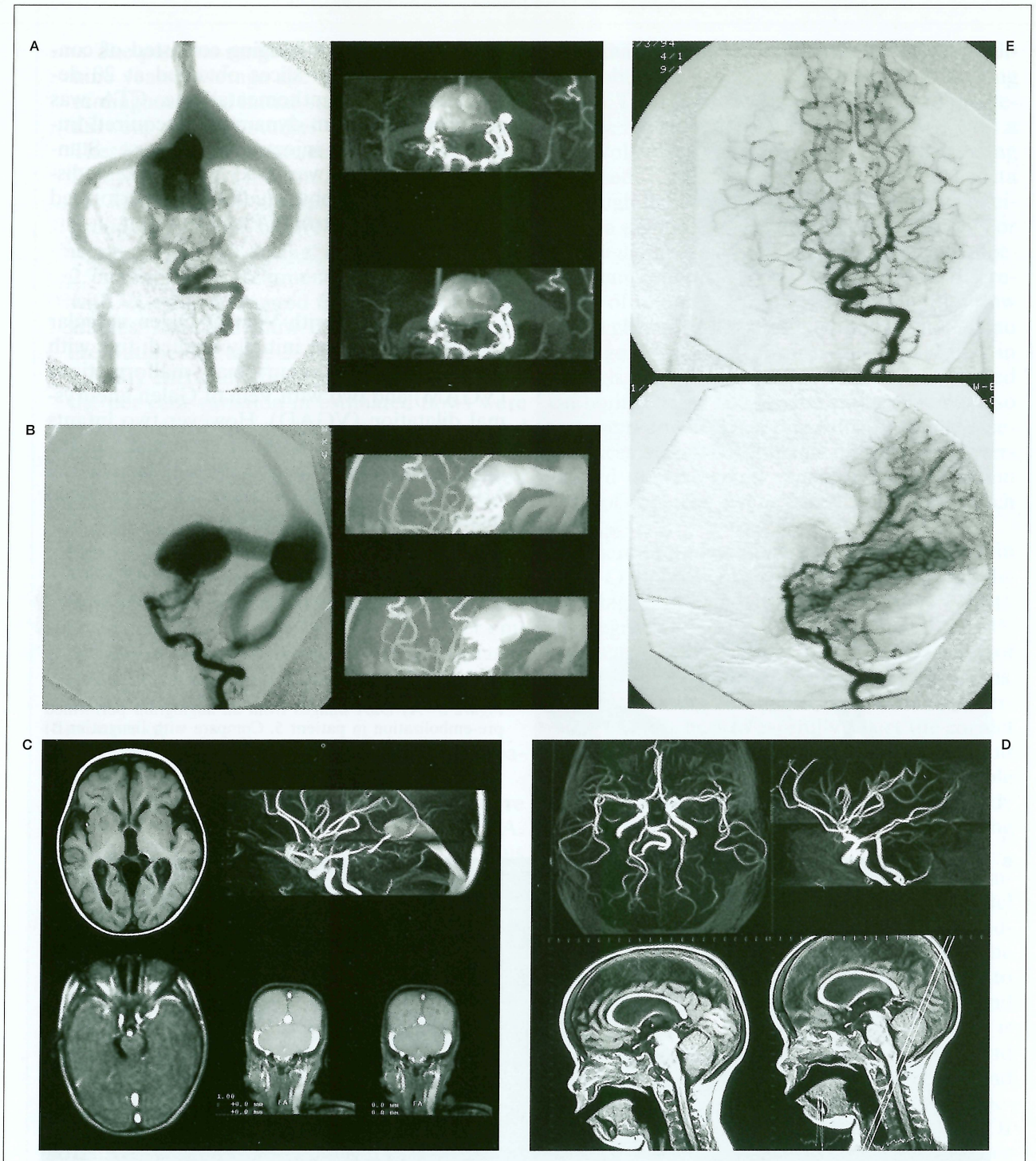
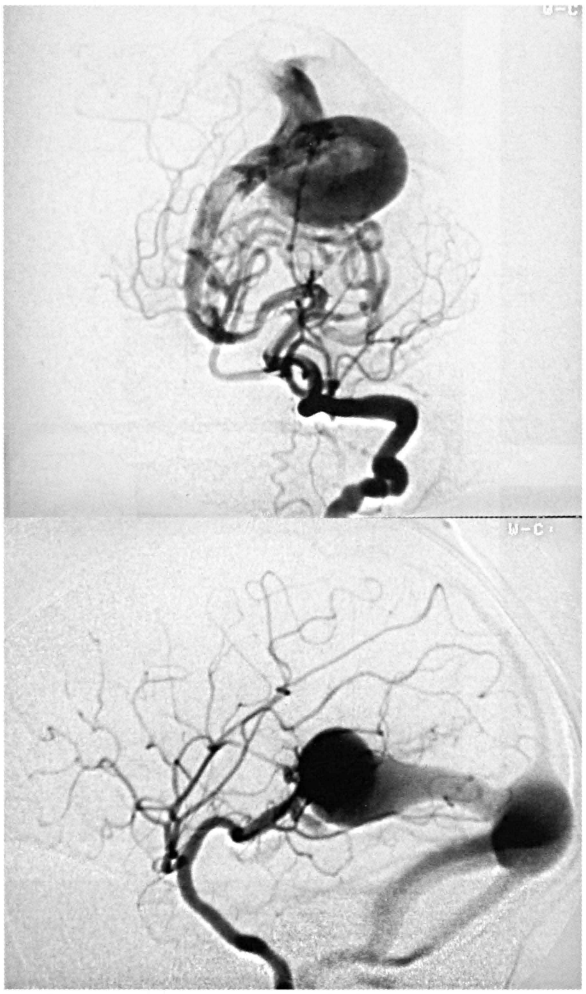


Figure 2 A) Composite frontal projections from a DSA and MRA performed on patient #4 on the same day. Note the accurate MRA representation of the feeding arteries. B) Composite lateral projections from and DAS and MRA that go with A. This arterial MRA sequence images the arterial and venous components of the VGAM. C) Same patient as in A,B above. This imaging occurred 7 months after embolization. The axial T1 image continues to show an enlarged median vein of the prosencephalon as does the MRA used for MR Q flow data. The lower right two images are oblique magnitude images from MR Q flow showing the signal from the draining vein and sigmoid sinuses. Flow was estimated at 326 ml/min, or 22% of cardiac output. D) Same patient as above imaged 20 months after treatment. Neither the MRA or standard T1 images show any significant residual venous flow. The lower right image shows placement of the sample volume for MR Q flow estimation, which showed a flow of 15 ml/min, or <1% of cardiac output. E) Control DSA frontal and lateral views for patient above show cure of VGAM.

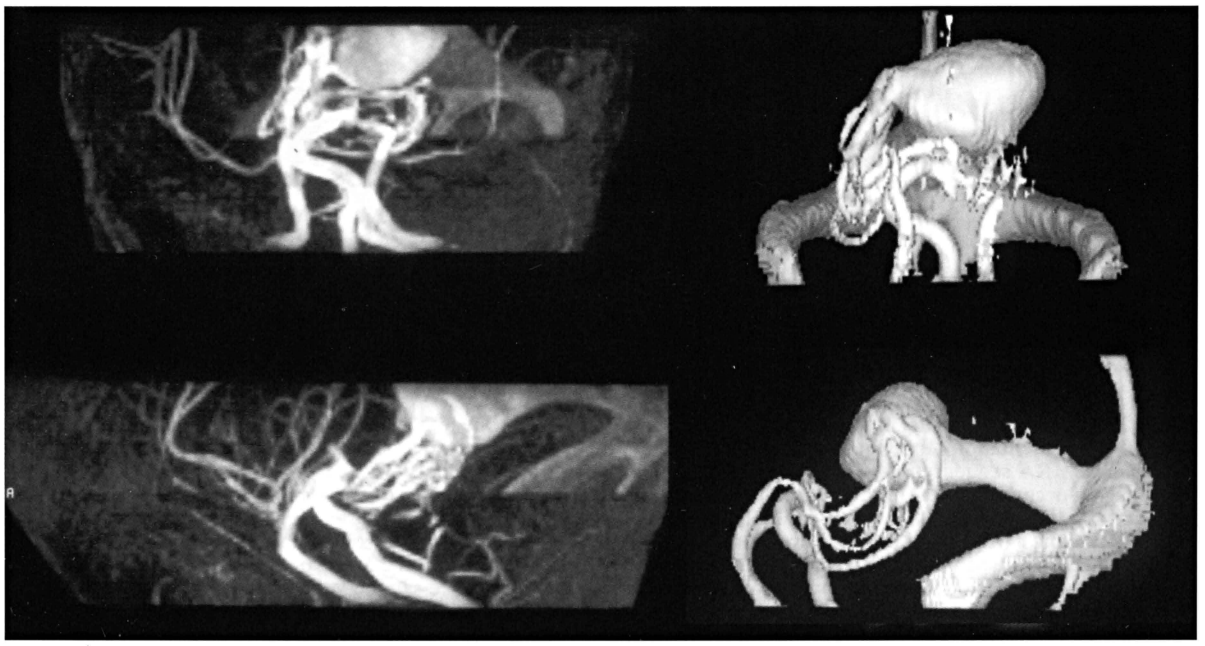


Iselin N.J.) Routine imaging consisted of contiguous axial 5 mm slices obtained at 20 degrees from the canthomeatal line. CTA was performed as 2 mm dynamically acquired images following the injection of contrast. Standard CT software was used for 3D image display. All angiographic studies were performed on a Siemens Polytron S/Plus DSA unit.

Results

Seven patients with Vein of Galen vascular malformations were initially studied; five with Vein of Galen aneurysmal malformations (VGAM) and two with Vein of Galen aneurysmal dilatation (VGAD). However two infants with VAGMs died without treatment in the early neonatal period and did not have serial MR flow data. These two infants have not been included in the data analysis.

Figure 3 A) DSA images from an angiogram performed pre-embolization in patient 5. Compare with images in B) Left images are from the MRA and right images from the CTA performed before the formal angiogram above. Note the accurate depiction of anatomy attained with these non-invasive methods. Management decisions were based on the CTA, MRA, and MR Q flow data.



The patients ranged in age from one day to nine years. (average age 1.5 years) at the time of diagnosis and initial study. The patients underwent multiple studies as shown in table 2. These studies were carried out over a period of five years and six months to eight years. Of the 15 MR Q Flow studies performed in this group, five were before treatment and ten were performed during or three months to 2.75 years after treatment. The three patients with VGAMs accounted for 12/15 MR Q Flow studies. The serial flow data from all patients are outlined in table 3. Between two to seven velocity encoded sequences were acquired and the per cent variation in estimated flows were calculated for the malformation and ranged between 2-9%.

MR Q Flow data from the VGAMs showed pre-treatment shunts ranging from 55-73% of cardiac output compared to 25-47% in the patients with VGAD. After embolization in VGAMs, there was an early reduction in shunt flow (64% in patient 4) and a significant delayed reduction of flow 15-26 months after embolization. With the reduction of the vascular shunts, total systemic cardiac output tended to return to the normal range of 150-200 ml/min/kg.

Figure 2 depicts some of the features for patient 4.

Ten out of fifteen angiographic studies were performed within one month of an MRA. MRA routinely captured arterial and venous flow, and correlated well with the corresponding angiograms, before and after treatment. Similarly the pre-treatment CTA studies were accurate depictions of the vascular anatomy identified by angiography at the time of embolization (figure 3).

Discussion

The idea of being able to accurately measure flow in vascular malformations is appealing. We believe that a validated technique will enable better timing of interventions such as embolization and allow the investigation of the natural history and post treatment follow up of vascular malformations such as VGAMs and VGADs. The first critical issue to be addressed is whether the derived data from MR Q flow techniques is accurate and reproducible.

MR phase contrast angiography relies on the fact that moving spins in a magnetic field gradient obtain a different phase than non-moving spins. The phase shift is proportional to the velocity, allowing MR to create an image with a controlled sensitivity to flow[8-11]. Cardiac gating is used to divide the phase encoded data through the cardiac cycle into increments in either a prospective or retrospective fashion. For through plane flow, the product of mean velocity (cm/s) and the pixel area (cm2) of the region of interest (ROI) will determine the flow through the ROI (cm3/s). Although there is no true gold standard for measuring blood flow in vessels, the MR technique has been validated in both in vitro and in vivo studies[3,4,11]. We also attempted to validate our velocity sensitive sequences before using them clinically and determined that we could expect an answer within 5% of the true value based upon our bench tests.

There are many potential sources of error in MR Q flow as errors may be introduced by aliasing, misalignment, partial volume effects, misregistration, phase shifts and signal loss[3,4,10]. Aliasing occurs because of the cyclic nature of phase with an inherent limitation of 2π radians. Post-processing can unwind some of these errors, but it is best to carefully select the correct velocity encoding (VENC) that does not result in aliasing. Thus we chose to run multiple VENC values when performing a clinical study and defined the lowest VENC without aliasing as the most accurate.

Misalignment occurs when the velocity encoded slice is not perpendicular to the vessel because velocity is only measured in the encoded direction. If the slice is oblique to the true direction of flow, the error is proportional to the cosinus of the angle between the flow and direction of encoding. In general the error is small over a broad range; 1% at 5 degrees and up to 6% at 20 degrees. If the background phase error is truly zero, then no flow error occurs in the estimate of flow since a larger ROI is generated to encompass the vessel. However we were able to obliquely orient in all three dimensions and place the sample slice in the direction of flow. Misregistration is caused by movement between slice selection, phase encoding and frequency encoding and if the slice is oblique to the direction of flow some of the signal will be displaced outside the vessel. This problem is also reduced by selecting a plane

Table 3

Patient	Age (yrs/mos)	# Venc	AVM (ml/min)	+ / – (%)	Cardiac Output	AVM/CO (%)	Systemic Cardiac Output (ml/min)	Cardiac Output per Kg
VGAD								
#1	9 yrs	5	2187	5	4260	47	2073	
#2	4 yrs 6 mos	3	617	3	2403	25	1786	105
	9 yrs	2	1200	8	-	-	-	-
VGAM								
#3	**EMBOLIZED DAY 1 OF LIFE**							
	1 mo	3	793	4	1422	56	629	112
	8 mos	3	718	3	1982	36	1264	114
	15 mos	7	204	9	1849	11	1645	113
#4	5 mos	3	1000	2	1800	55	800	101
	EMBOLIZED AT 5 MOS.							
	12 mos	3	326	4	1486	22	1160	105
	RE-EMBOLIZED AT 12 MOS.							
	20 mos	7	15	9	2350	<1	2335	163
	38 mos	2	<2	-	-	-	-	-
#5	3 wks	6	862	3	1180	73	318	99
	3 mos	4	926	5	1416	65	490	104
	EMBOLIZED AT 4 MOS.							
	7	2	400	4	-	-	-	-
	11	5	340	6	1309	25	969	106
	30	3	80	8	2073	4	1993	166

perpendicular to the flow and a sequence with short TEs.

With partial volume effects the mean velocity will be reduced but flow values will be correct if the background phase is zero since the resulting larger ROI will compensate. These effects are greatest with small vessels and thick slices and can be minimized by choosing a slice perpendicular to the flow and eliminating background phase errors. In our series of patients the sampled draining vein was large, ranging between 1 and 1.5 cm in diameter. This resulted in a sample ROI with 24-93 pixels with an average of 41 pixels, which is ample to eliminate the worries of partial volume effects. However, as the malformations involuted, the sampled vessel became progressively smaller and caused an increased variability in measurement as shown in table 3. The highest differences between VENC studies occurred with the lower flows but still remained small in absolute terms. For example in patient 5 the initial variability was 3% or 26 ml/min. and at three months the variability was 5% or 46 ml/min. These values are compared to 8% variability at 30 months (after treatment) which translates to a flow discrepancy of only 7 ml/min. Similarly, the highest variability of 9% was seen in two patients but translates into variability of flows of 2 and 18 ml/min.

Flow values are highly dependent on the background pixel values being correctly as-

signed a value of zero since this enables a generous ROI to encompass all of the flow from the vessel whether it is displaced or misaligned. Background phase errors may be caused by many factors including susceptibility effects, microcirculation effects, and MR design limitations such as RF instability, gradient repeatability, echo centering or echo sampling [10]. In general, background phase errors are less serious in the brain than in the chest. The lack of signal and random noise in the lungs translates into a greater challenge to find a background value of zero than occurs from the signal of the brain. We routinely measured the background phase errors in each case and found them to be less than 5 ml/min. in all cases. Usually the errors were less than 1 ml/min. and did not contribute any significant amount to the total estimated flows.

Differences in flow rates have been reported to be as great as 8-24% due to intra-observer variability in selecting ROIs [9]. Burkart describes an automated technique of vessel detection that shows less inter-user variability with an accuracy within 10% of true flow values in phantom tests. We believe our manual method of ROI generation is reliable and has been advocated by others [9]. It consists of using the magnitude images and setting the window width and levels at 50% of the maximal intraluminal signal intensity in the image. Magnification of the image allows for easier manual tracing of the ROI and care must be taken to include only the vessel in question. The generated ROI is then applied to the velocity map and each image is reviewed to ensure that vessel motion or distortion through systole and diastole is accounted for. ROIs of the background are generated to ensure that the phase errors are minimal.

There are many more potential sources of error and detailed discussion can be found elsewhere. [3,4,10-12]. It is clear that an MR system with superb gradient performance and the ability to place the sample slice in oblique planes are important factors in the success of MR Q flow. The very small background phase errors we encountered, the minimal variability among VENC sequences in the same study, and the good agreement with the angiographic studies and outcome of the patients lead us to believe that we have succeeded in accurately measuring flow in Vein of Galen vascular malformations.

The optimal time to embolize a VGAM is a balance between the neurodevelopment of the infant and the technical ease of the procedure. Berenstein and Lasjaunais [2] suggest that endovascular treatment may be postponed if strict monitoring assures that growth, neurological development and brain parenchyma on imaging all remain normal. Our data indicate that infants can cope with a vascular shunt/ cardiac output ratio of at least 70% without suffering CHF or neurological impairment. Repeated measurement of shunt flow may be a more objective indicator of the optimal time for endovascular treatment, but this question requires further study.

The flow data outlined in table 3 shows that in both cases of VGAMs that were treated with one intervention there was a delayed and significant reduction in flows. Early post-embolization flow studies showed reduction of shunt by up to 67% (Patient 4). However in patients 3 and 5 there was also a significant delayed reduction of flow 15-26 months after embolization without further treatment. Patient 4 was re-embolized 12 months after the first treatment, possibly too early to have seen the delayed reduction in flow that occurred in the other two patients, but the embolization resulted in 96% reduction of flow and predictable cure.

When discussing treatment of VGAMs Berenstein and Lasjaunias [2] write "embolization should be staged, because total occlusion is seldom achieved in one session due to the complex arterial supply" (307). Our data suggest there is a delayed involution of flow many months following embolization in VGAMs that is hard to ascribe to the initial treatment. It may be unnecessary to re-embolize until a significant length of time has passed after the first treatment and points out the strength of having an objective, noninvasive method of measuring treatment effects.

In our series the application of MRA, CTA and MR Q flow has resulted in a marked reduction in the number of angiograms performed on these children. For example, case five was diagnosed in utero at 32 weeks gestation and had the VGAM mapped by CTA and MRA at birth. The patient was also followed by MR Q flow until three months of age. The first angiogram was performed as part of the embolization session while a second angiogram was not performed until 30 months of age at

which time MR suggested she was cured. Unfortunately the patient also developed a dural type AV fistula which spontaneously involuted over the next year, but required two additional angiograms over the next five years.

MR Q Flow can measure flow in Vein of Galen vascular malformations. We believe that we have succeeded in our goal to develop an objective, non-invasive method of shunt quantification using velocity encoded MR sequences. In children with Vein of Galen vascular malformations we were able to reproducibly measure flows that were believable and in agreement with the clinical outcome and angiographic studies. This promises new insight into the hemodynamics, natural history and treatment response of vascular malformations.

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